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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 08/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/017,479	REENAN ET AL.	
	Examiner	Art Unit	
	Jon M. Lockard	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31,32,56,58,62-66,73,75-80 and 82-108* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31,32,56,58,62-66,73,75-80 and 82-108* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1647, Examiner Jon Lockard.

2. The previous examiner indicated allowable subject matter in a previous Office Action (mailed 04 December 2004). However, that Examiner has left the USPTO, and the indication of allowability is hereby withdrawn in view of the new rejections set forth below.

3. The Amendment filed 06 June 2005 has been received and entered in full. Claims 31, 56, 58, 62, 64-66, 73,75, 78, 82-84, have been amended, claims 53, 59, 61, and 67-71 have been cancelled, and claims 104-108 have been added. Therefore, claims 31-32, 56, 58, 62-66, 73, 75-80, 82-108 are pending and are the subject of this Office Action.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections and/or Rejections

Claim Rejections

5. The rejection of claims 53, 59, 64-71, 83, and 84 under 35 U.S.C. §112 ¶2 as set forth at page 3 in the previous Office Action (mailed 03 December 2004) is withdrawn in view of Applicant's amendments and cancellation of claims 53, 59, and 67-71 (filed 06 June 2005).

6. The rejection of claims 67 and 71 under 35 U.S.C. §112 ¶2 as set forth at page 3 in the previous Office Action (mailed 03 December 2004) is moot in view of Applicant's cancellation of said claims (filed 06 June 2005).

7. The rejection of claims 31, 53, 54, 58, 61-63, 67-71, 82-94, and 103 under 35 U.S.C. §112 ¶2 as set forth at pages 3-4 in the previous Office Action (mailed 03 December 2004) is withdrawn in part in view of Applicant's amendments and cancellation of claims 53, 54, 61, and 67-71 (filed 06 June 2005).

8. The rejection of claims 73 and 75-80 under 35 U.S.C. §112 ¶2 as set forth at page 4 in the previous Office Action (mailed 03 December 2004) is withdrawn in view of Applicant's amendments (filed 06 June 2005).

9. The rejection of claims 53, 59, and 64-67 under 35 U.S.C. §112 ¶1 as set forth at pages 4-5 in the previous Office Action (mailed 03 December 2004) is moot in view of Applicant's cancellation of said claims (filed 06 June 2005).

Maintained and/or New Rejections

Claim Objections

10. Claims 106-107 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The recitation of "further comprising selecting one or

more members..." in each of the claims does not further limit the subject matter of the claims from which they depend, but rather add an additional step.

Claim Rejections - 35 USC § 101 and 35 USC §112, 1st Paragraph

11. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.
>
> The following is a quotation of the first paragraph of 35 U.S.C. 112:
>
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim Rejections - 35 USC § 112, 1st Paragraph (New Matter)

12. Claims 83-103 and 108 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**. Claims 83 and 84 recite "detecting rate of aging of the cell", and claim 108 recites "measuring the lifespan of the cell". After extensive review, the Examiner is unable to find, in the Specification as originally filed, support for these newly added limitations in the claims. These newly added limitations are not expressly asserted, nor do they flow naturally from the Specification as originally filed. It is noted that the previous

Examiner suggested this claim language at page 3 of the previous Office Action (mailed 03 December 2004) so long as there was written support for the amendment in the specification.

13. Claims 31-32, 56, 58, 62-66, 73; 75-80, 82-108 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility. Novel biological molecules lack an established utility and must undergo extensive experimentation to determine an appropriate specific, substantial, and credible utility.

14. The instant application discloses an isolated Drosophila DNA sequence (INDY) set forth as SEQ ID NO:1 which encodes a protein comprising the amino acid sequence set forth as SEQ ID NO:2. The Specification teaches the Indy protein transports succinate, citrate, alpha-ketoglutarate, and fumarate (See Figure 12; pg 46, lines 10-16), and the transport is neither cation dependent (See Figure 15; pg 46, lines 17-27) nor sensitive to pH (See Figure 16; pg 47, lines 1-3). The Specification also teaches that the Indy protein is localized to the plasma membrane of midgut epithelial cells, fat body cells, and oenocytes (See Figures 11 and 12; pg 44, lines 25-29), with lower levels of the protein being found in the alimentary canals, base of the legs, and the third segment of the antennae (See pg 44, line 29 through pg 45, line 4). The Specification also teaches that the Indy protein shares substantial homology with rat sodium dicarboxylate cotransporters SDCT2 and SDCT1, and the human sodium dicarboxylate cotransporter hNaDC-1 (See pg 18, lines 10-15; Figure 9). The Specification teaches three mutants of the INDY gene in Drosophila results in an increase in the life-span of the fly carrying the mutation (See pg 7, lines 18; Figure 4) and a slower rate of "aging" in the fly (See Figure 8).

Based on these findings, the Specification asserts that Indy (Drosophila) mutants may be genetically calorically restricted, allowing them to eat normally, maintain high levels of physical activity and reproductive status, while benefiting from increased life-span. The Specification further asserts that the Indy protein can be used to identify drugs that interact with it to potentially block the uptake of key metabolites which would provide the benefit of increasing longevity through a form of caloric restriction and the control of ideal body weight (See pg 23, lines 13-22). However, the instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder, or physiological process which one would manipulate for a desired clinical effect. There is no well-established utility for a specific amino acid sequence and the specification fails to disclose a specific and substantial utility for the claimed invention.

15. The specification asserts the following as patentable utilities for the Indy polypeptide of SEQ ID NO:2:

1.) the Indy polypeptide can be used to screen for compounds which modulate its activity or its expression (pg 3, lines 19-25); and

2.) compounds which modulate the activity or the expression of the Indy polypeptide would be useful as therapeutics directed towards calorically restricting an organism, extending the life-span of an organism, hyperglycemia, diabetes, chronic obesity, metabolic disorders, or the symptoms of aging (pg 4, lines 4-7; pg 4, lines 7-10; pg 24, lines 18-20; and pg 38, lines 8-10).

16. These asserted utilities are not specific and substantial because they do not identify or reasonably confirm a "real world" context of use. The specification neither identifies the biological functions of the claimed protein nor any disorders that are associated with the claimed molecules. Clearly, further research would be required to determine the functions of the claimed

molecules or to identify a disease that can be treated or diagnosed with the claimed molecules which is insufficient to meet the requirement of 35 USC § 101.

17. The invention also lacks a well-established utility. A well established utility is a specific, substantial, and credible utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. Novel biological molecules lack an established utility and must undergo extensive experimentation to determine an appropriate specific, substantial, and credible utility. The identification of Indy as a carboxylate transporter does not endow the Indy polypeptide or the claimed methods of identifying a compound which binds to it or modulates its activity or expression with a specific and substantial utility.

18. The art teaches that sodium dicarboxylate cotransporters exhibit broad substrate specificities and carry a wide range of di- and tricarboxylic acids and have been localized in the epithelial cells of the renal proximal tubule, small intestine, colon, liver, placenta, and brain (Pajor, A.M. (1999). Sodium-coupled transporters for Krebs cycle intermediates. Annu. Rev. Physiol. 61:663-82; See page 664). Pajor also discloses that different sodium-coupled dicarboxylate transporters differ in substrate affinity and substrate specificity, and that individual transporters exhibit functional differences between species (See Table 1, pg 667, and pg 679). Thus, the identification of Drosophila Indy as a carboxylate transporter would not be accepted by those of skill in the art as being predictive of function. Utility must be in readily available form. It is possible that, after further characterization, this protein might be found to have a patentable utility, in which case proteins would have a specific utility, or the protein might be found to be associated with a specific disease. This further characterization, however, is part of the act of the invention, and until it has been undertaken, Applicant's claimed invention is incomplete.

Because the instant specification has failed to identify a physiological process which has been shown to be influenced by the activation or inhibition of the Indy transporter protein of the instant invention, an artisan would have no way of predicting what effects the administration of a compound which modulates its activity would have. If one cannot predict the effects that the administration of a ligand (i.e., modulator) of the Indy transporter protein of the instant invention is going to have on an organism, then it is unclear as to what practical or real-world benefit is derived by the public from the identification of that ligand (modulator).

19. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sup. Ct., 1966), in which a novel compound that was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be useful because the compound produced thereby was potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

While the discovery that mutations in the Drosophila Indy gene results in an increase in the life-span and a slower rate of "aging" of the fly carrying the mutation is a very interesting and

important scientific finding, it is not considered a "practical utility" under 35 U.S.C. § 101. In *Nelson v. Bowler*, the court reversed a finding by the Office that the applicant had not set forth a "practical" utility under 35 U.S.C. § 101, and stated: "Practical utility is a shorthand way of attributing "real-world" value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public". In the instant case, assertions that [b]ecause the Indy protein is isolated in regions of Drosophila that are involved in the metabolism and storage of fat, glycogen, and protein, and mutations in the Indy gene result in an increase in the life-span and a slower rate of "aging" of the fly carrying the mutation, compounds that are identified by the claimed methods can be used to treat hyperglycemia, diabetes, chronic obesity, metabolic disorders, or the symptoms of aging or to caloricaly restrict or extend the life-span of an organism, clearly establish that the instant invention cannot be used "in a manner which provides some immediate benefit to the public". To grant Applicant a patent encompassing methods of screening compounds which bind to or modulate the activity or expression of a transporter protein, which is not readily usable in its current form, would be to grant Applicant a monopoly "the metes and bounds" of which "are not capable of precise delineation". That monopoly "may engross a vast, unknown, and perhaps unknowable area" and "confer power to block off whole areas of scientific development, without compensating benefit to the public" (*Brenner v. Manson, Ibid*). To grant Applicant a patent on the claimed methods of screening compounds that bind to or modulate the activity or expression of the transporter proteins (Indy and 4 asserted homologs) based solely upon the finding that mutations in the Indy gene result in an increase in the life-span and a slower rate of "aging" of the fly carrying the mutation is clearly prohibited by this judicial precedent since the

compensation to the public is not commensurate with the monopoly granted. The instant claims are drawn to proteins which have undetermined function or biological significance. There is no evidence of record that would support a conclusion that compounds that bind to it or modulate the activity or expression of the proteins of the instant invention would be useful for treating hyperglycemia, diabetes, chronic obesity, metabolic disorders, or in methods of calorically restricting an organism or extending the life-span of an organism. Until some actual and specific activity or significance can be attributed to the protein identified in the specification as SEQ ID NOs:2-6, the claimed invention is incomplete. Furthermore, to employ a protein of the instant invention in the identification of substances which bind to it or stimulate or inhibit its activity or expression is clearly to use it as the object of further research, which has been determined by the courts to be a utility which, alone, does not support patentability.

20. Claims 31-32, 56, 58, 62-66, 73, 75-80, 82-108 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to make/use the claimed invention.

Claim Rejections - 35 USC § 112, 2nd Paragraph

21. Claims 31-32, 56, 75-80, and 83-108 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

22. Claims 31-32, 82-103 remain, and newly added claim 108, are rejected under 35 U.S.C. 112, second paragraph, for reasons set forth at pages 3-4 of the previous Office Action (mailed 03 December 2004). The claims are indefinite because it is unclear if the newly added limitation "has been expressed by a cell" refers to a polypeptide that is present in the cell or a polypeptide that has simply been expressed by a cell and, for example, now isolated or purified.

23. Claims 56, 66, and 104 are rejected as being indefinite because claim 56 does not have a step that clearly relates back to the preamble. For example, there is no step indicating the identification of a test molecule which interacts with a transporter protein.

24. Claims 75-80 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. In line 6 of claim 75, "assessing transport", does not set forth any steps involved in the method/process, therefore it is unclear what method/process is encompassed by the claim.

25. Claims 83-103 and 108 are rejected as being indefinite because the claims do not have a step that clearly relates back to the preamble. For example, there is no step indicating the identification of a test molecule which interacts with a transporter protein.

26. Claims 83-103 and 108 are further indefinite for reciting the phrase "contacting the test molecule to a cell" in the penultimate line of the claim. It is unclear whether "a cell" refers to the same cell mentioned in the first part of the claim or if it refers to a different cell.

27. Claims 83-103 remain and newly added claim 108, are rejected under 35 U.S.C. 112, second paragraph, for reasons set forth at page 3 of the previous Office Action (mailed 03 December 2004).

28. At page 12 of the response (filed 06 June 2005), Applicant states that the previous

Examiner recognized that symptoms of aging can be indicative of the rate of aging and argues that many such symptoms were well known in the art at the time of filing and are appropriate indicia for detecting the rate of aging.

29. Applicant's arguments have been fully considered but they are not persuasive for the following reasons. It is noted that Applicant has not provided any evidence or reference of record to substantiate the allegation that there are art recognized methods of detecting the "rate of aging" in the context of a cell. It must be emphasized that arguments of counsel alone cannot take the place of evidence in the record once an examiner has advanced a reasonable basis for questioning the disclosure. See *In re Budnick*, 537 F.2d at 538, 190 USPQ at 424; *In re Schulze*, 346 F.2d 600, 145 USPQ 716 (CCPA 1965); *In re Cole*, 326 F.2d 769, 140 USPQ 230 (CCPA 1964). For example, in a case where the record consisted substantially of arguments and opinions of applicant's attorney, the court indicated that factual affidavits could have provided important evidence on the issue of enablement. See *In re Knowlton*, 500 F.2d at 572, 183 USPQ at 37; *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979).

Thus, while the instant Specification provides a definition of "rate of aging" in the context of an organism (e.g., Drosophila), neither the Specification nor the art defines "rate of aging of a cell" unambiguously and therefore the metes and bounds of the claims cannot be determined.

Summary

30. No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback**, can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

JML
August 17, 2005

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER